REMARKS

Applicant respectfully requests reconsideration. Claims 1-21, 31-44, 57 and 59-61 were previously pending in this application. No claims have been canceled. Claims 1, 5, 8 and 31 have been amended. No new claims have been added. As a result, claims 1-21, 31-44, 57 and 59-61 are pending for examination with claims 1 and 31 being independent claims. Claims 57 and 59-61 are currently withdrawn. No new matter has been added.

Rejections under 35 U.S.C. §112

Claims 1-21, 31-44, 57 and 59-61 are rejected under 35 U.S.C. §112, first paragraph, for the reasons of record as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention. According to the Examiner, one would not readily envision any starting samples for use other than those containing IgG4 absent further guidance and predictable experimentation. In addition, according to the Examiner, the use of hydrophobic columns is not enabled.

Applicant respectfully traverses. The Examiner has not provided a reasonable basis by which to question the enablement of the scope of the claims as directed to the separation of IgG immunoglobulins of an isotype other than IgG4. The Examiner has attempted to argue that immunoglobulin isotypes other than IgG4 are not known to predictably produce mixtures of half and whole antibodies. In support of this argument, all that is referred to in the cited references is merely the alleged teaching that IgG4 differs from other IgG human isotypes. This falls far short from establishing that non-IgG4 immunoglobulins do not produce mixtures of half and whole antibodies. In fact, the cited references do not teach that non-IgG4 immunoglobulins do not dissociate into half and whole antibodies. Further, the Examiner has provided no convincing arguments as to why non-IgG4 immunoglobulins cannot form a mixture of half and whole antibodies and has also provided no arguments as to why a mixture of half and whole antibodies of immunoglobulins other than IgG4 cannot be separated by the methods of the claimed invention.

Nevertheless, even if, *arguendo*, immunoglobulins of an isotype other than IgG4 cannot dissociate into half and whole antibodies, which Applicant does not concede is the case, the

presence of such embodiments does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments would be inoperative or operative with the expenditure of no more effort than is normally required in the art. (MPEP §2164.08). The Examiner has not demonstrated that undue experimentation is required.

The Examiner has also argued that the use of hydrophobic columns is not enabled for reasons of record. In the previous Office Action (mailed 11/03/2006), the Examiner states that the ability of hydrophobic interaction columns to capture and selectively release half and whole antibodies is not in evidence and would seem unpredictable absent further guided experimentation. However, the Examiner has provided no arguments as to why the use of hydrophobic columns *seems* unpredictable. Since enabling support for the use of hydrophobic columns is provided in the instant application (See, *e.g.*, pages 4, 5 and 8-12) and the use of hydrophobic columns for the separation of proteins is routine in the art, the Examiner has not met his burden of establishing a *prima facie* rejection that the claimed invention is not enabled for the use of hydrophobic columns. The statement that the use *seems* unpredictable is not sufficient to establish a *prima facie* rejection.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §102

Claims 1-4, 10, 12-15, 20 and 21 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by King et al. (*Biochem. J.*, 281: 317, 1992) in light of Colcher et al. (Cancer Res 49: 1783, 1989) and either Schuurman et al. (Molecular Immunol 38: 1, 2001) or the instant disclosure. The Examiner refers to arguments presented in the previous Office Action. In addition, according to the Examiner, King et al. teaches that the Protein A-sepharose and ion exchange chromatography method of Colcher et al. was used for purification of the IgG4 mixtures. Furthermore, according to the Examiner, this method involved lowering of the pH. Finally, according to the Examiner, Applicant's previous arguments were unpersuasive because recitations of "intended use" have no patentable weight.

Applicant respectfully traverses. King et al. do not provide all of the limitations of Applicant's claims. Applicant's claims recite that half and whole antibodies are separated, a feature the Examiner has conceded is not provided by King et al. In his obviousness rejection (page 5 of

the Office Action), the Examiner has indicated that King et al. do not teach methods that result in the separation of half and whole antibodies as provided in Applicant's claimed methods. Such separation is required by Applicant's claims and is not merely a recitation of an intended use with no patentable weight. Further, King et al. do not teach obtaining a sample that contains a mixture of IgG half antibodies and IgG whole antibodies of the same isotype and *reducing the pH of the sample* such that the half antibodies dissociate from one another to form a resulting solution that contains dissociated IgG half antibodies and IgG whole antibodies. King et al. also do not teach reducing the pH of the sample *prior* to applying the sample to the column. The method of Colcher et al., which according to the Examiner was used by King et al., provides a step of running a pH gradient *after* applying an antibody sample to a column.

Finally, Applicant notes that the Examiner briefly mentions Schuurman et al. and the instant disclosure without fully describing how these references serve to support this rejection. Nevertheless, in light of the fact that King et al. do not provide the methods of Applicant's claims, there is no need to address how Schuurman et al. or the instant disclosure may support this rejection.

Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Claims 1, 2, 5, 8, 9, 12 and 20 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Palmer et al. (*Biochem. J.*, 3: 863, 1964). According to the Examiner, Palmer et al. teach reduced rabbit IgG prepared from serum samples to produce a proportion of half IgG molecules in the preparations, pH reduced to dissociate the non-covalent interactions of the half IgG molecules, and reduced and lowered pH sample applied to a column to separate the half IgG and whole IgG molecules.

Applicant respectfully traverses. Palmer et al. do not anticipate the claimed invention. Palmer et al. do not teach obtaining a sample that contains a mixture of IgG half antibodies and IgG whole antibodies of the same isotype and *reducing the pH of the sample* such that the half antibodies dissociate from one another to form a resulting solution that contains dissociated IgG half antibodies and IgG whole antibodies. The teachings of Palmer et al. relate to the preparation of a reduced immunoglobulin, which comprises a low pH condition as part of the reduction protocol. Palmer et al. do not teach lowering the pH of a sample that contains a mixture of IgG half antibodies

and IgG whole antibodies. Therefore, for at least these reasons, the reference does not anticipate the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

Claims 1-5, 8-21 and 31-42 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combined teachings of King et al. (*Biochem. J.*, 281: 317, 1992), Schuurman et al. (*Molecular Immunol.* 38: 1, 2001), Angal et al. (*Mol. Immunol.* 30: 105, 1993) and Palmer et al. (*Biochem.* 3: 863, 1964). According to the Examiner, King et al. teach mixtures containing IgG4 half and whole antibodies and applying the mixtures to a series of columns including ion exchange columns. Further, according to the Examiner, King et al. teach the desirability of separating half from the whole antibodies but do not teach separating the antibodies other than by SDS gel electrophoresis. In addition, according to the Examiner, Schuurman et al. suggest that the non-covalent interactions of half antibodies can be dissociated by denaturing conditions, such as by low pH. Further, according to the Examiner, Palmer et al. teach the dissociation of the non-covalent interactions of half IgG molecules by low pH and size exclusion chromatography for the separation of dissociated half from whole IgG. Also, according to the Examiner, Angal et al. suggest partial resolution of non-mutated half and whole antibodies by ion exchange chromatography but provides no details therefore.

Applicant respectfully traverses. The combined teachings of King et al., Schuurman et al., Angal et al. and Palmer et al. do not result in the claimed invention. Neither King et al. nor Schuurman et al. nor Palmer et al. teach obtaining a sample that contains a mixture of IgG half antibodies and IgG whole antibodies of the same isotype and *reducing the pH of the sample* such that the half antibodies dissociate from one another to form a resulting solution that contains dissociated IgG half antibodies and IgG whole antibodies. Angal et al. do not provide the missing teaching. Thus, for at least this reason, King et al., Schuurman et al., Angal et al. and Palmer et al., separately or in combination, do not render obvious the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: January 14, 2008

Respectfully submitted,

By_____

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